

COMPARISON OF IONTOPHORETIC LIDOCAINE TO EMLA CREAM FOR PAIN  
REDUCTION PRIOR TO INTRAVENOUS CANNULATION IN ADULTS

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## ABSTRACT

The insertion of intravenous (IV) catheters, required for most operative anesthesia, can be a source of pain and anxiety. Lidocaine, a local anesthetic, is frequently injected intradermally to decrease pain associated with IV cannulation in adults. Topically administered EMLA (Eutectic Mixture of Local Anesthetics) cream is frequently used, but it takes one hour for it to effectively anesthetize venipuncture sites, which limits its usefulness. A method gaining acceptance in healthcare is the iontophoresis (transdermal administration of ionizable drugs utilizing an electric current) of a polarized local anesthetic. Using iontophoresis, a local anesthetic such as lidocaine, a positively charged molecule, can be used to effectively anesthetize the skin to depths of up to 8mm without the use of needles, in as few as ten minutes.

The purpose of this study was to compare the iontophoresis of lidocaine with epinephrine to EMLA cream for producing local anesthesia prior to intravenous cannulation. A descriptive study utilizing the experimental method with a cross over design was used. The procedures for the study consisted of the random application of EMLA cream (for 60 minutes) or the iontophoresis of 4% lidocaine HCl (40 mg/ml) with 1:50,000 epinephrine (20 mcg/ml) (40 milliamp minutes) to either the dorsal surface of the right or left hand. Results were that the iontophoresis of 4% Lidocaine HCl with Epinephrine 1:50,000 (20 micrograms/millimeter (mcg/ml) reduced pain more effectively than EMLA cream associated with intravenous cannulation in adults (14 mm vs. 3 mm for the EMLA cream and Iontophoresis respectively). The majority of subjects preferred iontophoresis.

Key Words: **Iontophoresis, EMLA Cream, Lidocaine HCl, Epinephrine, Visual Analog Scale, Intravenous Cannulation, Adults, Pain, Anesthesia**

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by

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## **DEDICATION**

I dedicate this thesis to Debra, my wife, and my parents, Terry and Jackie Spence. Their love and support have given me the ability to obtain any dream, and without them my dreams would be meaningless.

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## CHAPTER I: INTRODUCTION

### Background

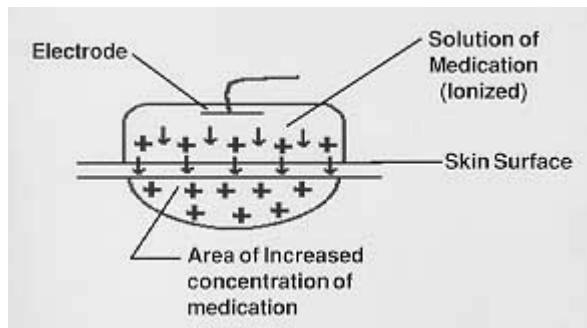
Intravenous (IV) access by means of a large bore catheter is required for most operative anesthesia procedures. During the preoperative period, the insertion of intravenous catheters is frequently a source of pain and anxiety for patients. To promote patient comfort and satisfaction, anesthesia providers often inject a local anesthetic intradermally at the insertion site prior to insertion of the catheter. However, infiltration of local anesthetics can be uncomfortable.

Topical eutectic mixture of local anesthetics (EMLA) cream, an alternative to intradermal injection for decreasing pain associated with intravenous cannulation, has been shown to effectively anesthetize the venipuncture site when applied topically one hour prior to venipuncture (Gajraj, Pennant, & Watcha, 1994). However, the lengthy application time limits its usefulness in the preoperative setting. Therefore, there is a need for a method that produces topical anesthesia in a short period of time, works on intact skin, without systemic side effects, and invokes neither pain nor discomfort. One such method that meets these criteria is iontophoresis of polarized local anesthetics.

Iontophoresis is the process of introducing ionic, polarized drugs into the skin of the body via electric current for therapeutic purposes. Veratti, in 1747, originated the use of an electric current to increase the penetration of electrically charged particles into surface tissue (Chien & Banga, 1989). Since that time, there have been numerous reports about iontophoresis of various medications. The historical background of iontophoresis and its current uses will be explored in chapter two.

The principle behind iontophoresis is very simple. It is a method of delivering a

medication to a localized tissue area by applying a direct electrical current to an electrolyte solution containing ionic molecules, which in turn is applied to the area to be treated (Bang & Chien, 1988). The mechanism behind iontophoresis is also simple: similar electrical charges repel each other. Therefore, a positive current will drive positively charged drug molecules away from the electrode and into the tissues, as depicted in Figure 1; likewise a negative current will drive negatively charged drug molecules into the tissues. A local anesthetic such as lidocaine, a positively charged molecule, can be utilized in this manner to effectively anesthetize the skin to depths of up to 8 mm without the use of needles (Irsfeld, Klement, & Lipfert, 1993).



**Figure 1. Diagram of the Mechanism of Iontophoresis**

EMLA Cream is a mixture of 2.5% lidocaine and 2.5% prilocaine. It works by diffusing through intact skin to block neuronal transmission from dermal receptors (Gajraj et al., 1994). Many studies have shown it to be very effective in preventing pain associated with venipuncture both in children and adults (Soliman, Lynn, Broadman, Hannallah, & McGill, 1988; Hallen & Uppfeldt, 1982). However, to be effective, it must be applied to intact skin at least 60 minutes before the procedure and covered with an occlusive dressing. This may limit its usefulness in the operating room.

Studies on the iontophoresis of lidocaine have shown it a very effective method in reducing the pain of needle insertion in as little as 10 minutes (Gangarosa, 1981; Ashburn

et al., 1997). However, studies are lacking in the literature that compare iontophoresis of lidocaine with epinephrine to EMLA cream for local anesthesia prior to venipuncture.

Therefore, the purpose of this study was to compare the iontophoresis of lidocaine with epinephrine to EMLA cream for producing adequate local anesthesia prior to intravenous cannulation.

### Research Questions

1. Does iontophoresis of 4% Lidocaine HCl with Epinephrine 1:50,000 (20 micrograms/millimeter (mcg/ml) reduce pain more effectively than EMLA cream to intravenous cannulation in adults?

2. Is iontophoresis of 4% lidocaine HCl with Epinephrine 1:50,000 or EMLA cream preferred by adults before intravenous cannulation?

### Conceptual Framework

The conceptual framework of this research was based on two theories. The first theory is Imogene King's Theory of Goal Attainment (Evans, 1991), and the second is the neurophysiological theory of pain, more specifically the anterolateral system, and its associated fibers. In addition, the theory of action of local anesthetics will be presented.

#### King's Theory of Goal Attainment

Imogene King's (as cited in Evans, 1991) theory of goal attainment provides a strong foundation for this research study, as well as for the practice of nurse anesthesia. The theory focuses on the interpersonal relationship between the nurse and the client. The phenomena of concern in this theory is based on processes and outcomes. The process is mutual goal setting between the nurse and the client, and the outcome is the goal to be obtained that can be measured by a change in behavior.

In King's (as cited in Evans, 1991) theory, the context by which goal attainment occurs is as follows. The nurse and the client do not know each other. The client is in need of nursing care. The nurse is in a position because his or her knowledge level, to provide a service to the client. The nurse and client communicate with each other and agree to a means to identify problems or concerns and set mutual goals to resolve those concerns. The nurse and client purposefully interact to achieve the mutually set goals, and this interaction occurs in its natural setting.

Six variables were identified by King (as cited in Evans, 1991) that lead to the relationship between the nurse and the client. These variables will be described as they apply to nurse anesthesia. (1) One member of the nurse client dyad initiates a behavior. This behavior could be the nurse anesthetist informing the patient he or she needs an IV for surgery. (2) The opposite member of the dyad responds with behavior, and (3) a problem is noted in the dyadic situation. This problem is that patients do not want to experience pain or discomfort. (4) A goal is mutually agreed upon by members of the dyad. This goal can be the anesthetist describing a method (iontophoresis of lidocaine) to insert the IV painlessly to the patient. (5) An exploration of means to achieve the goal is initiated by one member of the dyad, or behavior is exhibited by member of dyad that moves toward goals; (6) and other member agrees with means to achieve the goal. In this example, the patient agrees to proceed with the iontophoresis, the anesthetist proceeds with the procedure and successfully prevents pain while the IV is inserted into the patient.

This theory is very applicable to anesthesia as well as to this research study. For example, the setting could be the preoperative holding area; the anesthetist communicates

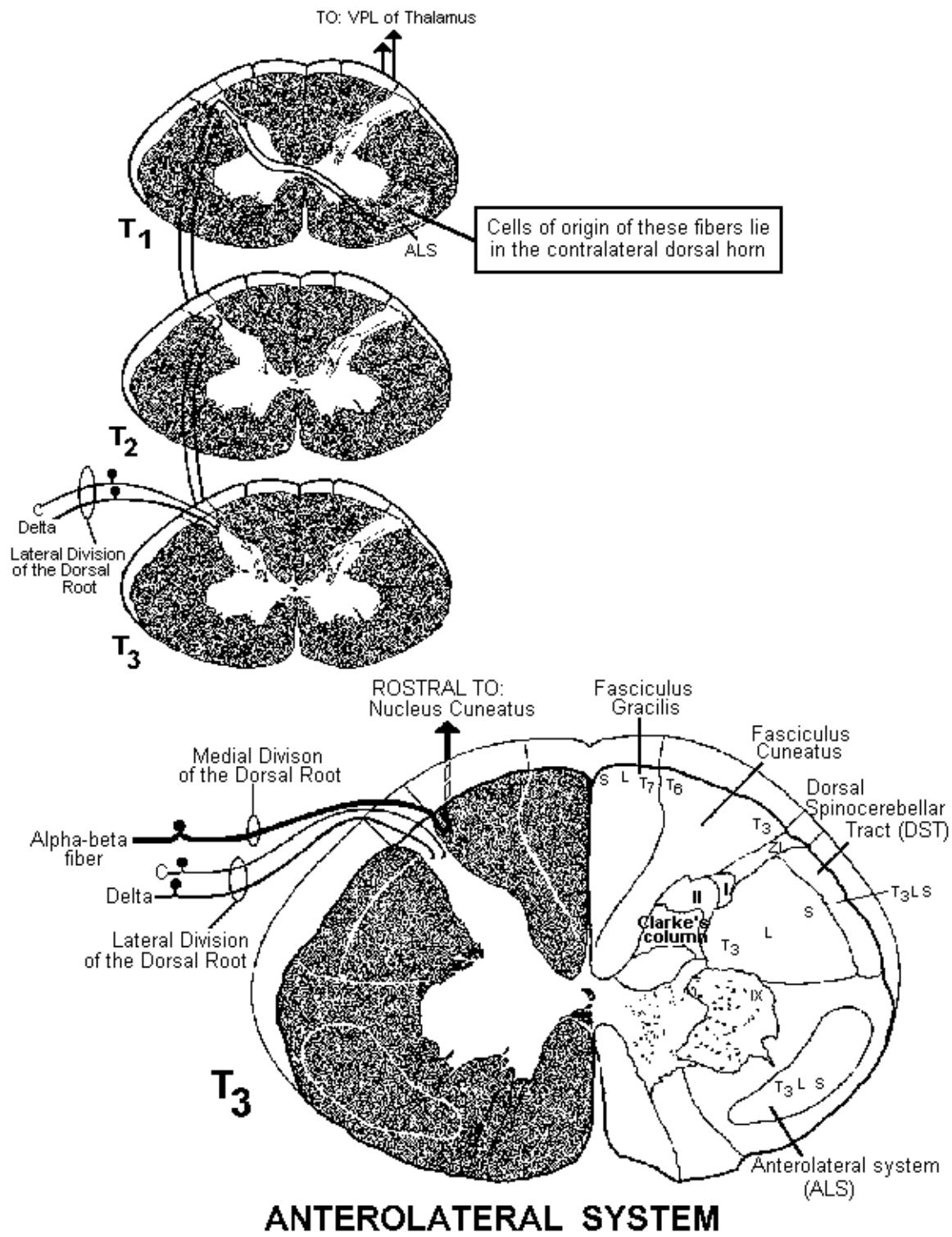
to the patient the need for an intravenous catheter for surgery, and describes the procedure to the patient. The patient communicates to the nurse verbally or non-verbally his desire not to experience pain. The anesthetist works with the patient to set a mutual goal to achieve this outcome. The anesthetist asks the patient if he or she would be willing to proceed with this procedure if it was painless. The patient agrees and, a mutual goal has been set to achieve a desired outcome. If the anesthetist is successful in reducing the patient's pain, and he or she was satisfied with the method, then the goal has been obtained. In this particular scenario, iontophoresis is the process to achieve the goal and the lack of pain during IV cannulation is the outcome.

### Neurophysiology Theory of Pain

Intravenous cannulation causes tissue damage and a pain impulse is registered in the central nervous system. To understand how the body responds to this painful event, one must first understand the afferent pain pathways. Nociceptors are receptors that respond to intense, tissue damaging stimuli. They carry their receptor signals over a variety of A-delta and C-neuronal fibers, which are extensively supplied not only to the cutaneous tissue, but also to underlying muscle and fascia. The A-delta fibers are fast conducting (12-30 m/s), thinly myelinated (diameter, 2-5 m) fibers that respond to sharp pricking pain impulses. C-fibers are slow conducting (0.4-1.2 m/s), unmyelinated fibers (diameter, 0.3-1.3 m) that respond to slow, dull pain impulses. The A-delta fibers are sometimes referred to as the first or fast pain fibers, and the C-fibers as the second or slow pain fibers.

A pain impulse, such as tissue damage following IV cannulation stimulates the A-delta and C fibers in the cutaneous tissue to send impulses to the spinal cord via the

dorsal roots of the spinal nerves to the dorsal horn of the spinal cord. Prior to synapsing in the dorsal horn these fibers ascend or descend one or two spinal cord segments via Lissauer's tract (see Figure 2). The impulses of the A-delta fibers synapse primarily on neurons in lamina I and V and the C fibers synapse on neurons in lamina II and III of the substantia gelantosia of the spinal cord. Substance P is one neurotransmitter that is released by these fibers at their synaptic connections. Interneurons send the impulses to the spinothalamic tract cells, which cross anterior to the central canal in the ventral white commissure and course rostrally in the anterolateral funiculus (Gilman & Newman, 1996). Once in the brain stem these fibers synapse in the reticular formation, thalamus, and other neural groups. The pain impulse may also be transmitted to the postcentral gyrus of the parietal lobe where the pain is interpreted in the primary somatosensory cortex, and a response occurs. There are several other critical areas, which receive the nerve impulses.

Figure 2. An Illustration of the Spinothalamic Tract.

### Action Potentials

The purpose of the peripheral nerve is to carry information to or from the brain and spinal cord. This is accomplished via electrical signals called action potentials. The speed of the action potential is based on the fiber diameter of the nerve. Larger myelinated fibers, such as the A-delta, transmit nerve impulses much faster than smaller unmyelinated fibers, such as C-fibers.

To understand how an action potential works, one must first understand basic cell physiology. The basic plasma membrane is a bilipid layer in which water and most water-soluble ions cannot pass through. Embedded in the membrane are certain channels that are selective for various ions such as sodium and potassium. Some of these channels are nongated, gated by voltage, membrane potential, chemical transmitter, or mechanical distortion (Bryant, 1997). The nongated channels are primarily responsible for maintaining the resting membrane potential, which is normally  $-90\text{mV}$  in large alpha motor neurons (Butterworth & Strichartz, 1990). The voltage gated sodium and potassium channels control the propagation of the action potential.

Ions diffuse through these channels under the influence of electrical and chemical forces. Potassium has a high concentration on the inside of the cell and a low concentration on the outside; therefore, it tends to want to diffuse down its concentration gradient out of the cell, causing repolarization of the cell. However, when it leaves the cell it leaves behind negatively charged anions that cannot pass through the lipid membrane. These negatively charged ions create an electrical gradient that tends to pull in positively charged ions such as sodium. Sodium, whose concentration is high on the

outside and low on the inside, tends to want to also diffuse down its concentration gradient into the cell interior. This causes the cell to depolarize, and the membrane potential becomes more positive.

An action potential is generated when the nerve cell is depolarized above the threshold potential for the cell. The threshold potential is the point at which the action potential will be generated. This is sometimes referred to as an all or nothing phenomena. When it occurs, voltage gated sodium channels in the cell membrane open, increasing the membrane permeability to sodium causing sodium activation. The sodium ions rush into the cell, down its electrical and concentration gradient, through these open channels and cause depolarization. At the peak of the action potential, the voltage gated sodium channels begin to close and sodium inactivation occurs, and voltage gated potassium channels slowly begin to open and potassium begins to leave the cell interior. The positively charged potassium ions leaving the cell cause the cell to hyperpolarize, and it brings the membrane potential back toward the resting potential.

The action potential is propagated by the inward sodium current flowing ahead of the action potential and depolarizing the nerve cell membrane to threshold, producing a new action potential (Bryant, 1997; Butterworth & Strichartz, 1990). Local anesthetics, such as lidocaine and prilocaine, work by blocking the transmission of nerve impulses to the brain. They do this by impairing propagation of the action potential. This is achieved when the local anesthetic binds to one or more of the receptors located in the sodium channel, which prevents the sodium ion influx needed for initiation and propagation of the action potential (Carpenter & Mackey, 1997). This slows the rate of depolarization of the nerve action potential such that the threshold potential is not reached, as seen in figure

3, and thus no pain or sensory impulses are transmitted to the spinal cord (Stoelting & Miller, 1994).

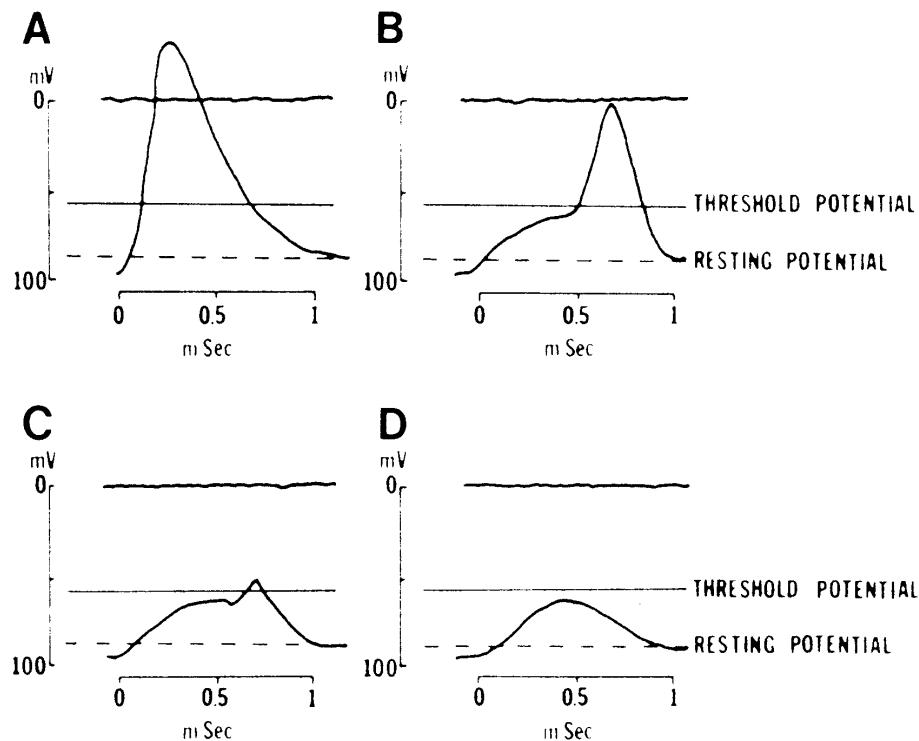


Figure 3. Local Anesthetics Affect on Compound Action Potential: Effect of 0.2 mmol/L lidocaine on nerve membrane action potential. (A) control recording; (B,C, and D) recordings following exposure to lidocaine. (Covino, 1976)

The conceptual framework for this research has been presented. King s (as cited in Evans, 1991) theory of goal attainment has also been presented. The neurophysiology theory of pain and the spinothalamic tract have been described. The methods by which an action potential is generated and stimulates the transmission of nerve impulse have been presented. Finally, the theory of action of local anesthetics has been discussed.

### Variables of Interest

The major research variables are:

1. Independent variables:

Iontophoresis

Lidocaine

Epinephrine

EMLA cream

2. Dependent Variables:

Pain

3. Measurement Tools:

Visual Analog Scale

### Definition of Terms

For the purpose of this study the following terms have been conceptually and

operationally defined:

1. Iontophoresis: The method of transdermal administration of ionizable drugs in which electrically charged molecules are propelled across the skin by an external electric field. **Operational definition**: The amount of current delivered in a set period of time. Current in millamps multiplied by duration in minutes= mA min. This is equivalent to the amount of drug administered. 1.75 cc of 4% Lidocaine HCL and 0.25 cc of Epinephrine 1:50,000 at a current of 3-4 millamps for 10-15 minutes for a total drug delivery of 30-60 millamp minutes. Current and duration were based on patient tolerance.

2. Lidocaine: A local anesthetic used to produce infiltration anesthesia and epidural and peripheral nerve blocks. **Operational definition:** 1.75 cc of 4% Lidocaine HCl.
3. Epinephrine A synthetic drug utilized as a vasoconstrictor, antispasmodic, and sympathomimetic. **Operational definition:** 0.25cc of 1:50,000 (.005 mg) concentration of Epinephrine. Its purpose in this study was to increase the duration of action of lidocaine. (see Appendix A)
4. EMLA Cream: A eutectic mixture of local anesthetics. An ointment that contains local anesthetics so that topical application causes local anesthesia without the need for injection. **Operational definition:** 6 cm of 2.5% Lidocaine and 2.5% prilocaine, that will be applied to the dorsal surface of each subject's right hand.
5. Eutectic mixture: When a combination of drugs mixed together have a lower melting point than the melting point of the individual drugs. EMLA is such a combination, which is a liquid at room temperature, and the individual components are crystalline solids.
6. Pain: A subjective feeling of distress, suffering, or agony caused by stimulation of specialized nerve endings. An unpleasant sensory and emotional experience arising from actual or potential tissue damage or described in terms of such damage. **Operational definition:** Pain will be quantified by 10 centimeter (cm) long horizontal, visual analog scale, marked by the subject indicating his or her level of pain. The distance from the left end of the scale to the respondent's mark is measured in millimeters, and this number is recorded

7. Visual Analog Scale: A scale widely used by anesthesia providers when assessing the intensity of acute pain in clinical research. **Operational definition**: A 10-cm horizontal line with anchors at each end of the scale. The left end of the scale has the anchor no pain (0 cm), while the right end of the line has the anchor pain as bad as it could possibly be (10 cm) . (see Appendix B)

8. IV cannulation: The procedure by which a catheter is inserted into a vein for the purposes of medication administration. **Operational definition**: For the purposes of this study a successful cannulation was noted by a blood return into the needle hub of an 18-gauge angiocatheter.

### Assumptions

The following assumptions was pertinent to this study:

1. All subjects had intact neurological systems, and were able to perceive, and respond to painful stimuli in a physiologic manner.
2. Pain is an undesirable experience.
3. The subjects were honest in their comments on the two methods of producing topical anesthesia.

### Limitations

The following limitations were pertinent to this study:

1. The subjects were not blinded to the treatment methods administered.
2. No placebo was used.

## CHAPTER II: REVIEW OF THE LITERATURE

### Introduction

In the following pages, a historical overview of the development of Iontophoresis and its current uses today in healthcare will be presented. Research studies on the use of iontophoresis of lidocaine for dermal anesthesia, from the past 17 years, will be presented. Finally, a brief review of the current uses of EMLA cream will be presented, as well as research studies on its efficacy.

### Historical Overview

Chien and Banga (1989) provided an excellent review of the historical overview of the use of iontophoresis. The idea of using an electrical current to deliver charged drugs across surface tissues was originated by Veratti in 1747. Morton, in 1898 wrote about an experiment in which he used an electrical charge to deliver graphite into his arm. At the turn of the 20<sup>th</sup> Century, Leduc performed the first well-documented experiment of iontophoresis in which he introduced strychnine and cyanide into two rabbits with a direct current. Ichihashi, in 1936, began using iontophoresis for the treatment of hyperhydrosis. Harris, in 1957, used iontophoresis of local anesthetics for the treatment of trigeminal neuralgia. Gibson and Cooke, in 1959, used lidocaine and pilocarpine iontophoresis to diagnose cystic fibrosis. Since then, this procedure has been approved by the FDA, and now widely used to diagnosis cystic fibrosis. Finally, in the 1980s research began into the use of iontophoresis for the delivery of drugs systemically for the treatment of various disorders.

There are a variety of health related disciplines that are using iontophoresis in clinical practice. Physical therapy, dermatology, otorhinolaryngology, ophthalmology,

and dentistry are some of the more documented disciplines in the literature (Banga & Chien, 1988). Many of these disciplines are using iontophoresis for the administration of local anesthesia before surgical procedures. For example, iontophoresis has become a preferred method by some providers for local anesthesia of the eardrum in myringotomy. In addition, many studies have documented local anesthesia of the skin to depths of 1.0 cm or more in human volunteers (Gangarosa, 1993). Recently, iontophoresis has been tested for pain control for a variety of diseases, and for postoperative analgesia (Ashburn et al., 1992). Gangarosa (1993, pg. 164) noted, Whenever an ionic drug is available for an appropriate surface condition, the drug can be optimally delivered by electrical assistance.

#### Research Studies on Iontophoresis

Gangarosa (1981) performed a study to determine the practical and effective concentration of lidocaine and epinephrine to use for local anesthesia of the skin. He compared several local anesthetics with and without epinephrine to topically applied anesthetics for the grade of anesthesia, duration, depth of needle penetration, and vascular activity. Sequential analysis was used as the method of comparison. The best results were obtained with the iontophoresis of 2-4% lidocaine with epinephrine 1:10,000 to 1:50,000. The current used was 1 mA for 10 minutes. Gangarosa also noted lidocaine to be far superior to procaine, tetracaine, mepivacaine and bupivacaine for local anesthesia of the skin.

Arvidsson, Ekroth, Hansby, Lindholm, and William-Olsson (1984) were concerned that the pain of venipuncture was hindering people from coming back as blood donors. In a randomized, double blind study of 47 regular blood donors, they compared

the iontophoresis of 20% lidocaine (200mg/ml) to a placebo. Pain was classified on a three-grade scale in comparison to a previous experience. The authors noted an 89% reduction in pain for the treatment group and 28% for the placebo.

Russo, Lipman, Comstock, Page, and Stephen (1980) compared the duration and depth of anesthesia produced by the iontophoresis of 4% lidocaine to subcutaneous injection of lidocaine and topical application of 4% lidocaine. Phase one of their study was a two factor, randomized, double blind study of 27 subjects. The iontophoresis of lidocaine was compared to lidocaine infiltration, topical lidocaine, or placebo iontophoresis for the duration of anesthesia. In phase two, the depth of needle penetration with a suture was measured in 12 subjects after lidocaine iontophoresis. A paired t-test was utilized and the results were highly significant,  $p < 0.001$ . The mean duration of anesthesia for the iontophoresis was 14.5 minutes and 22.2 minutes for the infiltration method. The problem with this study was that no site was monitored for more than 40 minutes. Overall, they reported the lidocaine applied by iontophoresis was more effective in producing skin anesthesia than applied by topical application, but analgesia duration was shorter than that provided by the infiltration method. They concluded that lidocaine iontophoresis was an effective method of producing local anesthesia for about five minutes without the use of local infiltration.

Irsfeld et al. (1993) performed an experiment to compare the efficacy of EMLA cream to that of iontophoretically applied 5% lidocaine with 1:50,000 epinephrine to pain on intravenous venipuncture and injection of hyperosmolar saline. Their study consisted of six adult volunteers in which pain was induced by a 27-gauge cannula during venipuncture. Hyperosmolar saline (2500 milli-osmols/ kg) was used for the injection

method. The depth of anesthesia was determined at five different sites by the use of a 27-gauge cannula until pain or discomfort was felt. A visual analog scale was used to measure the pain on injection. Wilcoxon s signed rank test was used for statistical analysis, and the results were significant ( $p<0.05$ ). Pain on injection was significantly reduced by iontophoresis, than the EMLA cream. The depth of needle penetration was deeper for the iontophoresis, with a mean of 6.0 mm, range 4.8-7.4mm, than EMLA cream, mean 4.4mm, range 3.2-4.8mm. No difference in duration of anesthesia was noted for either method. They noted that transdermal local anesthesia by iontophoresis reduced pain on IV injection of hyperosmolar saline, whereas venipuncture was painless with both methods. They also noted that since the iontophoresis of lidocaine reduced the pain of hyperosmolar injection of saline that it must deliver the molecules much deeper into the skin to block the vein wall afferents.

Ashburn et al. (1997) evaluated the clinical safety and effectiveness of iontophoresis of 2% lidocaine HCL with epinephrine 1:100,000 to induce local anesthesia before intravenous (IV) cannulation. This was a two-section study. The first section consisted of seven healthy adults who underwent iontophoresis to determine plasma lidocaine concentrations, and any adverse effects from this concentration of lidocaine and epinephrine. No detectable blood levels of lidocaine were noted after a dose delivery of 40ma/min, and the adverse effects were minimal. The clinical phase of the study was a randomized, double blind; placebo controlled study of 44 patients who required an IV before outpatient eye surgery. The purpose was to document the degree of analgesia to IV cannulation, and the patient s acceptance of the procedure. The results were that pain was decreased with the iontophoresis, it was well accepted by the patients, and the

adverse effects were minimal. A 10-cm visual analog scale was used to assess the pain. The mean was 0.7 for the iontophoresis group and 2.1 for the placebo group. They noted that iontophoresis of 2% lidocaine with 1:100,000 epinephrine for short delivery times does not lead to important systemic levels of lidocaine. In addition, they stated that this method of iontophoresis provides adequate skin anesthesia for placement of small-peripheral gauge IV catheters.

Zeltzer et al. (1991) compared iontophoresis of 4% lidocaine with 1:50,000 epinephrine to subcutaneous infiltration of lidocaine for local anesthesia. This study was performed on 13 pediatric patients, age ranges 11-19, who were undergoing hemodialysis. The purpose was to assess the children's responses to these two methods of anesthesia delivery, to evaluate their acceptability and efficacy for reducing pain and anxiety associated with dialysis needle insertion. A 10-cm visual analog scale was used to measure pain, anxiety, and satisfaction during the procedure. The dose of iontophoresis was 30 mA/min. Each child received both methods at three separate times. Three different raters patient, nurse and observer, rated each variable. The results indicated that iontophoresis was not significantly less painful than the infiltration method, and anticipatory anxiety decreased over time only for the infiltration method. Iontophoresis was less painful than subcutaneous injection. For dialysis needle insertion, the iontophoresis was not as effective as the infiltration method for reducing the pain. The authors postulated that disillusionment with iontophoresis was one reason for this result. They also noted that although iontophoresis was the less effective of the two methods, that it was met with more satisfaction than the injection method. A problem noted by the researchers in this study was the large attrition rate due to adverse effects

from the iontophoresis. Three patients dropped out by time three because of complications related to the iontophoresis, two with burns and one because of the prolonged time of administration for the iontophoresis. In the discussion, it was stated that iontophoresis of local anesthetics needs further investigation before it can be recommended as an alternative method of drug delivery in children.

#### EMLA Cream

EMLA cream is a combination lidocaine 2.5% lidocaine and 2.5% prilocaine. For many years in Europe, EMLA cream has been widely used as a topical anesthetic prior to venipuncture in children. It has now gained widespread use in the U.S. EMLA cream is predominately used for both venipuncture, and venous and arterial cannulation. EMLA cream has also led to a change in the practice of pediatric IV inductions in many countries in which this product has been available. Now intravenous inductions, as opposed to inhalation inductions are gradually becoming the technique of choice for this age group (Gajraj et al. 1994). Other clinical uses of EMLA cream include: lumbar puncture, epidural injections, drug reservoir injections, skin surgery, genitourinary surgery, ear, nose, throat, oral surgery, lithotripsy, and there are some anecdotal reports of its use for the treatment of postherpetic neuralgia.

Hallen, Carlsson, and Uppfeldt (1985) performed a double blind, randomized study of 31 adult volunteers to determine the efficacy of EMLA cream to a placebo in obtunding the pain produced by venipuncture. Pain was measured on a 10-cm visual analog scale. Each subject was to receive five applications of EMLA and three of the placebo. Both applications were applied for one hour, and then venous blood samples were subsequently drawn. The results noted that 28 of the subjects had lower pain scores

with EMLA than the placebo, and in the remaining three, EMLA and the placebo were equally effective in reducing pain. The authors noted that these results confirm similar results from previous studies performed on the analgesic effect of EMLA cream.

Smith, Gray, Ingram, and Jewkes (1990) performed a double blind study of the efficacy of EMLA cream in alleviating the pain of arterial cannulation. EMLA cream was compared to infiltration with lignocaine (lidocaine). The sample consisted of 40 adults, who were randomly assigned to receive one of four treatments. EMLA cream alone, EMLA cream and 0.9% saline infiltration, EMLA and 1% Lignocaine infiltration, or placebo cream and 1% Lignocaine infiltration. The application time was 60 minutes for the EMLA cream. Pain was measured on a visual analog scale by the patients. A four-category verbal rating scale was used by an independent observer after arterial cannulation. The results were significantly lower pain scores ( $p<0.01$ -patient; observer  $p<0.001$ ) in all patients who received EMLA cream when compared to the placebo or infiltration group. The authors noted that this study demonstrates that EMLA cream is useful for alleviating the pain associated with arterial cannulation in unpremedicated adults.

Bjerring and Arendt-Nielsen (1990) performed a study to determine the depth and duration of analgesia to needle insertion produced by EMLA cream application. The study consisted of 12 healthy volunteers. Application times were 30, 60, 90, or 120 minutes. Sensory and pain thresholds were determined by inserting an 18-gauge needle perpendicular through the anesthetized skin every 30 minutes for four hours after removal of the EMLA cream. Needle depth measurements were also done. Statistical analysis was done by Wilcoxon s test with a significance level of  $p<0.05$ . The results indicated

that sensory and pain threshold depths measured immediately after removal of the EMLA cream increased linearly for increasing application time. Maximal dermal depths of analgesia (approx. 5mm) were obtained 30 minutes after a 90-minute application or during the 60-minute period following the two-hour application of local anesthetic.

### Summary

In this chapter, a historical background of iontophoresis, its current uses in healthcare, and research studies from the past 17 years were presented. Previous research has demonstrated the ideal concentration of lidocaine and delivery current to adequately produce topical anesthesia. The majority of the research on iontophoresis has compared iontophoresis to infiltration of lidocaine, topical lidocaine or placebo methods. These studies have shown its efficacy in producing adequate anesthesia for venipuncture, as well as anesthesia to tissue depths of up to 1cm. Ashburn et al. (1997) demonstrated that iontophoresis is a safe and effective means of producing local anesthesia for venipuncture, with minimal adverse effects. In addition, studies have demonstrated EMLA cream to be effective in producing local anesthesia of the skin within 60 minutes for venipuncture. However, few studies have been done that directly compare the iontophoresis of lidocaine with epinephrine to EMLA cream to determine which method is more effective in producing topical anesthesia. Only one study, by Irsfeld and colleagues (1993), directly compared these two methods of producing topical anesthesia. The study showed that the iontophoresis of Lidocaine reduced the pain of noxious stimuli whereas EMLA cream did not. No study to date compares the two using IV catheter insertions as the noxious stimuli. Thus, there is a gap in the knowledge about these two methods of producing local anesthesia that this study will address.

### CHAPTER III: METHODOLOGY

#### Research Design and Procedures

To answer the question, Does the iontophoresis of 4% lidocaine (40 mg/ml) with epinephrine 1:50,000 (20 mcg/ml) reduce the pain associated with IV cannulation more effectively than EMLA cream in adults? A pilot study utilizing the experimental method with a crossover design was used.

In this study, each subject served as his or her own control (crossover design). The procedures for the study consisted of the random application of EMLA cream or the iontophoresis of 4% lidocaine HCl (40 mg/ml) with 1:50,000 epinephrine (20 mcg/ml) to either the dorsal surface of the right or left hand. The application time for each treatment was consistent with the manufacture recommendations. The EMLA cream was applied under an occlusive dressing (Tegaderm) for 60 minutes, as recommended by the manufacturer, prior to intravenous cannulation. The iontophoresis procedure was consistent with the Life-Tech local Anesthesia protocol, as depicted in Appendix A, which consists of using 2-4% lidocaine and epinephrine 1:10,000-1:200,000. A current of 4 mA was used for a period of 10 minutes. The current was slowly increased, according to the subject's comfort level, to maximum of 4 milliamps for a total delivery time of 10 minutes. This equated to a delivery current of 40 milliamp minutes (current X duration = delivery current). After completion of the treatment measures, an 18 gauge intravenous angiocatheter was inserted into a suitable vein under the treatment site by the principle investigator. This size angiocatheter was selected because this is the standard size IV catheter used on adult patients in the operating room for fluid volume replacement. The insertion of the angiocatheter was randomized among subjects as to

which hand receives the venipuncture first.

Immediately after a flash back of blood was noted in the needle hub of the angiocatheter, the subject was asked to rate their pain level associated with IV cannulation using a 10-cm horizontal Visual Analog Scale (VAS). In addition, each subject was asked to describe their preference concerning the two treatment methods on a piece of paper. This added a qualitative method to this study, and allowed the investigator to identify common variables among subjects, and helped answer the second research question: Is iontophoresis of 4% lidocaine HCl with Epinephrine 1:50,000 or EMLA cream preferred by adults before intravenous cannulation?

#### Equipment and Materials Utilized

The iontophoresis was initially completed utilizing the Microphor™ Iontophoretic applicator, model number 6121, and Meditrode drug delivery electrodes manufactured by Life-Tech, Inc. (1998, Houston, TX). During the initial data collection process with this unit, inconsistent results (will be presented in chapter four) were discovered. Life-Tech, Inc. was contacted, and a new unit, the Iontophor-PM/DX™ applicator was obtained for the final data collection. The Microphor™ unit was sent back to Life-Tech, Inc. for testing. The lidocaine utilized was a commercial preparation of 4% lidocaine HCL (40 mg/ml) (Astra Pharmaceuticals, Westborough, MA), Epinephrine 1:50,000 (20 mcg/ml) was added to this preparation prior to the treatment began. The amount of Lidocaine HCl used was a total of 1.75 ml, which equals 70 mg. The dose of epinephrine used was a total of 0.25 ml, which equals 5 mcg. The EMLA cream (Astra Pharmaceuticals, Westborough, MA), was the standard 2.5% Lidocaine HCl and 2.5% Prilocaine commercial mixture. The dose of Lidocaine HCl in EMLA cream is 25 mg per gram and

for Prilocaine is 25 mg per gram. For this study, a total of 2.5 grams was either placed over a 6-cm area on the dorsal surface of the subjects right or left hand. This equaled a total dose of 62.5 mg of Lidocaine HCl and Prilocaine. Sterile 18 gauge-1.16 inch angiocatheters (Becton Dickinson, Sandy, UT) were utilized for the venipuncture.

#### Sampling

This study took place in a pre-selected room at the Uniformed Services University of the Health Sciences (USUHS). After institutional review board approval, a convenience sample of 29 adult volunteers participated in this study. The initial 15 subjects participated in the initial data collection utilizing the Microphor™ iontophoresis unit prior to equipment problems being identified. Another 14 subjects were enrolled utilizing the Iontophor-PM/DX™ unit, and a new data collection process began. Neither coercion, nor compensation was used to recruit volunteers. All subjects were students from the Graduate School of Nursing Students at USUHS. Informed consent (see Appendix D) was obtained from all subjects prior to data collection.

#### Measurement Methods

A 10-cm horizontal VAS (see Appendix B) was utilized to quantify the pain response to IV cannulation. Each subject marked his or her level of pain on this scale immediately after a flash back of blood was noted in the needle hub. The distance from the left of the scale to the subject's mark was recorded in millimeters. In addition, each subject was asked the following question (see Appendix C). Please describe the adequacy of the treatment measures you just received, and comment on how effective you thought each method was, as well as any preference you may have.

### Validity

The validity of an instrument is the degree to which that instrument measures what it is intended to measure. The very subjective nature of pain makes it difficult to adequately quantify pain. Numerous studies have been done to demonstrate the validity of the VAS. A study performed by Ohnhaus and Adler (1975) compared the verbal rating scale (VRS) to the VAS and noted the correlation between the two instruments to be highly significant,  $r=0.81$ ,  $p<0.001$ . The authors felt that the VAS assessed more closely what a patient actually experiences with respect to change in pain intensity than the verbal rating scale. Scott and Huskisson (1976) attained similar results; the VAS correlated well with other measures of methods of measuring pain. Taenzer (1983) noted a significant correlation between the McGill Pain Questionnaire and the VAS, noting that both of these methods are valid and appropriate methods for assessing pain. Therefore, sufficient studies have been done to adequately justify the validity of the VAS as a method of assessing pain intensity.

### Reliability

Reliability is defined as the degree to which an instrument consistently measures characteristics for which it was designed to measure. The reliability of the VAS has been demonstrated (Aitken, 1969; Huskission, 1983). Huskission (1979) noted a correlation coefficient of 0.99 between successive measurements of pain on a VAS, and thus reproducibility is not a problem. Revill, Robinson and Hogg (1976) using the test-retest method obtained correlations of 0.95-0.99 when they asked subjects to remember a distant pain after five minutes and 24 hours. Therefore, the reliability of the VAS has been demonstrated using a variety of techniques.

### Protection of Human Rights

Participation in this study was voluntary, and participants were free to withdraw at any time if they desired, without jeopardy to themselves. Participants were required to give informed consent to voluntarily participate in this study, prior to beginning the procedure (see Appendix D). As part of the consent procedure, each subject was assessed for any allergies to the local anesthetics being utilized in this study. Subjects found to have sensitivity to local anesthetics were excluded from the study. In addition, any subject with skin imperfections on his or her hands was excluded. These imperfections include moles, scars, warts, or damaged skin.

The VAS and the comment form were numerically coded at the top, rather than listing the name of the individual on the form, in order to treat obtained data with anonymity and confidentiality.

The risks associated with the treatment measures included temporary erythema/blanching of the iontophoretically treated site, and minor stinging or burning sensations. Potential adverse risks also included failure to cannulate the vein, bruising at the intravenous site, failure to produce adequate analgesia, and potential allergic reactions to local anesthetics were all potential adverse risks.

### Data Analysis

Data collection consisted of pain scores utilizing a VAS. Data analysis was accomplished using inferential statistics. The sample size for this study was originally planned to be 20 adult subjects for each treatment variable. The desired sample size, based on Kraemer and Thiemann (1987) table for a paired t-test, was 18 subjects per group. Sample size calculations were based on the following assumptions:

1. A power analysis of 0.80
2. An alpha or significance level of 0.05
3. Medium to large effect size

. However, due to equipment problems, the final sample in the Iontophor-PM/DX group consisted of 14 adult subjects. An unpaired t-test was used with an alpha level at 0.05 to test the differences between mean VAS scores. The software utilized for data analysis was SPSS version 8.0 for Windows 98 (1998).

## CHAPTER IV: ANALYSIS AND INTREPRETATION OF DATA

### Introduction

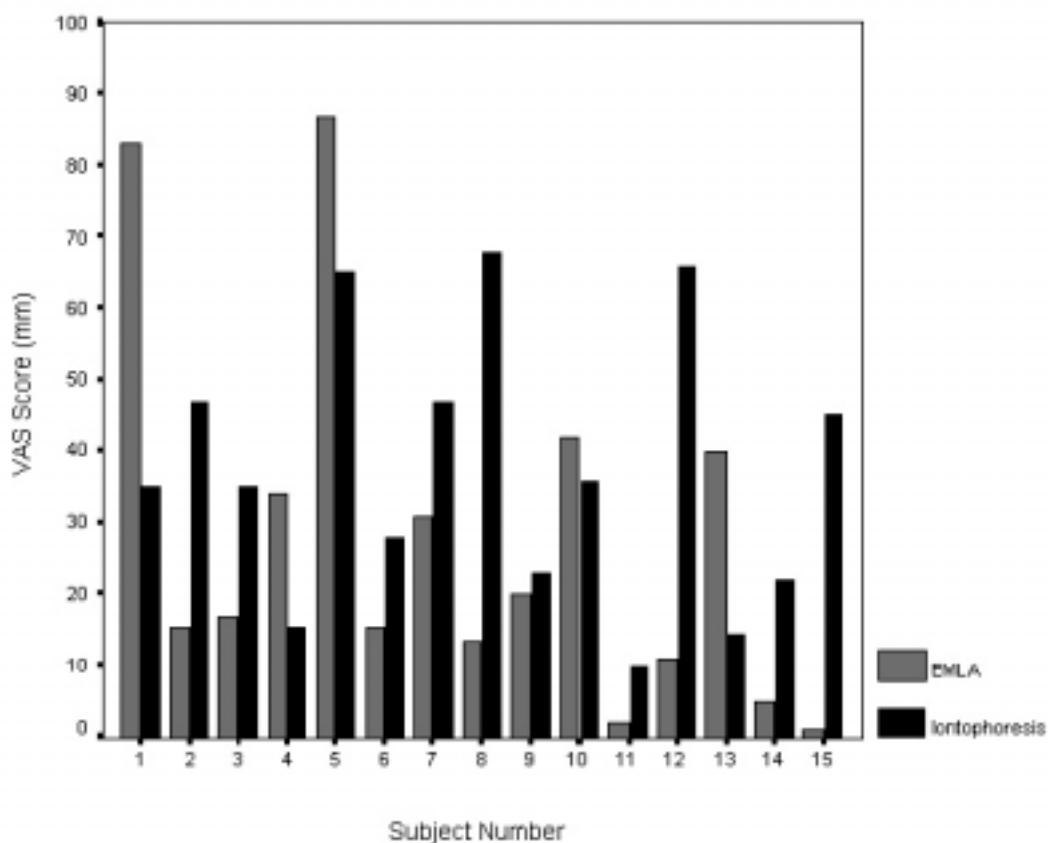
In this chapter the results of data collection will be presented. Initial data from the MicroPhor™ Iontophoretic Drug applicator , will be presented as well as data collected utilizing the Iontophor™-PM/DX unit™. An analysis of the data will be provided.

The purpose of this study was to compare the efficacy of iontophoresed lidocaine and topically applied EMLA cream, in producing local anesthesia prior to IV cannulation in adults. An initial convience sample of 15 adult volunteers enrolled in the study, but the results were not consistent with data analysis. A new convience sample of 14 adult volunteers was enrolled in the study. Each subject received an application of 2.5 grams of EMLA cream and iontophoresed 4% lidocaine HCl with 1:50,000 epinephrine to the dorsal surface of either the right or left hand. EMLA cream was applied 60 minutes prior to intravenous cannulation. Iontophoresed 4% lidocaine HCl with 1:50,000 units of epinephrine was applied for 11 minutes at current of 4 milliamps, prior to intravenous cannulation. After both treatments were completed, an 18-gauge angiocatheter was inserted into a suitable vein, under the treatment sites, by the principal investigator. Immediately after a flash back of blood was noted in the hub of the angiocatheter, subjects were asked to rate the pain associated with the IV cannulation on a 10-cm horizontal VAS. Subjects were also asked to provide written comments about the two treatment measures and to state which treatment they preferred.

### Data Analysis: MicroPhor™

A total of 15 student volunteers enrolled in this study in which the MicroPhor™

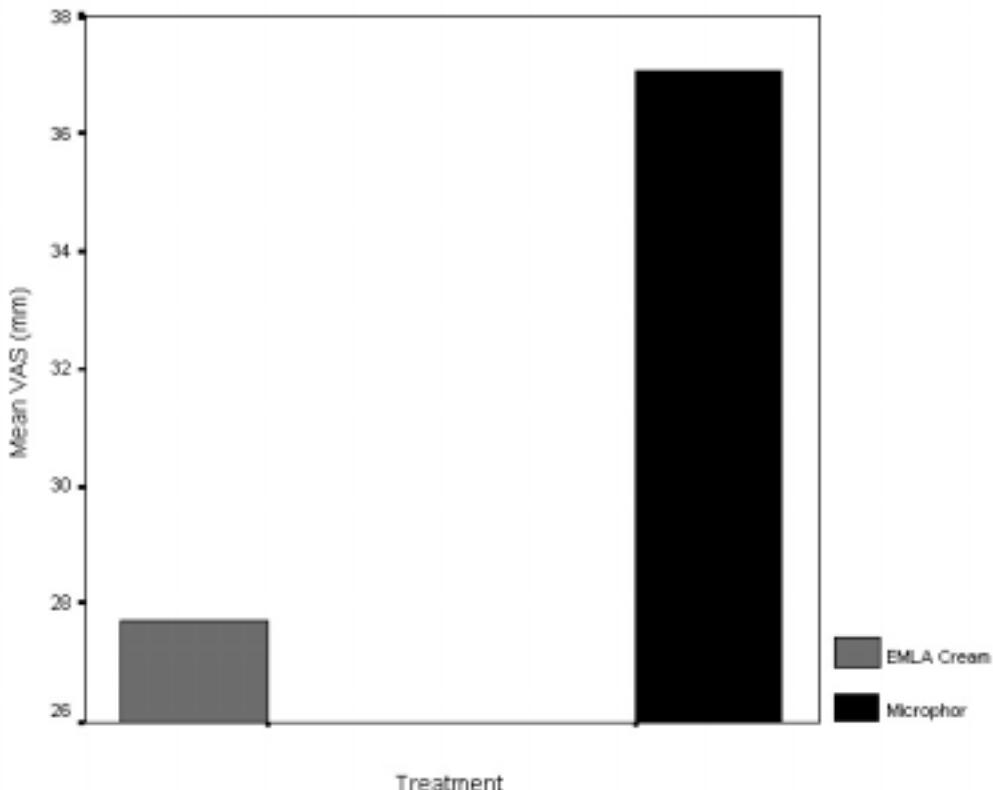
Iontophoretic Drug applicator was used, ten male and five female volunteers. Each treatment was randomized as to the right or left hand of each volunteer, as well as which hand received the venipuncture first (iontophoresis or EMLA Cream). The EMLA cream application was placed 60 minutes prior to the venipuncture. The iontophoresis procedure began at 50 minutes after the EMLA cream was applied, and it consisted of a total dose delivery of 40 mA/minutes (electric current was set at 0.0 mA and was increased to a maximum of 4.0 mA for 10 minutes). Results of the initial data are presented in Figures 4 and 5.



**Figure 4.**

**Visual Analog Scale Scores for Pain with Veinpuncture for the Microphor™**

**Iontophoresis Unit and EMLA Cream.**



**Figure 5.**

**Mean VAS Score: EMLA Cream vs. Microphor“.**

The mean VAS scores for the EMLA group was 27 mm (S.D. 26 mm). The mean VAS score for the Iontophoresis group was 37 mm (S.D. 19 mm). The wide variation in scores in both groups is demonstrated in Table 1.

**Table 1**

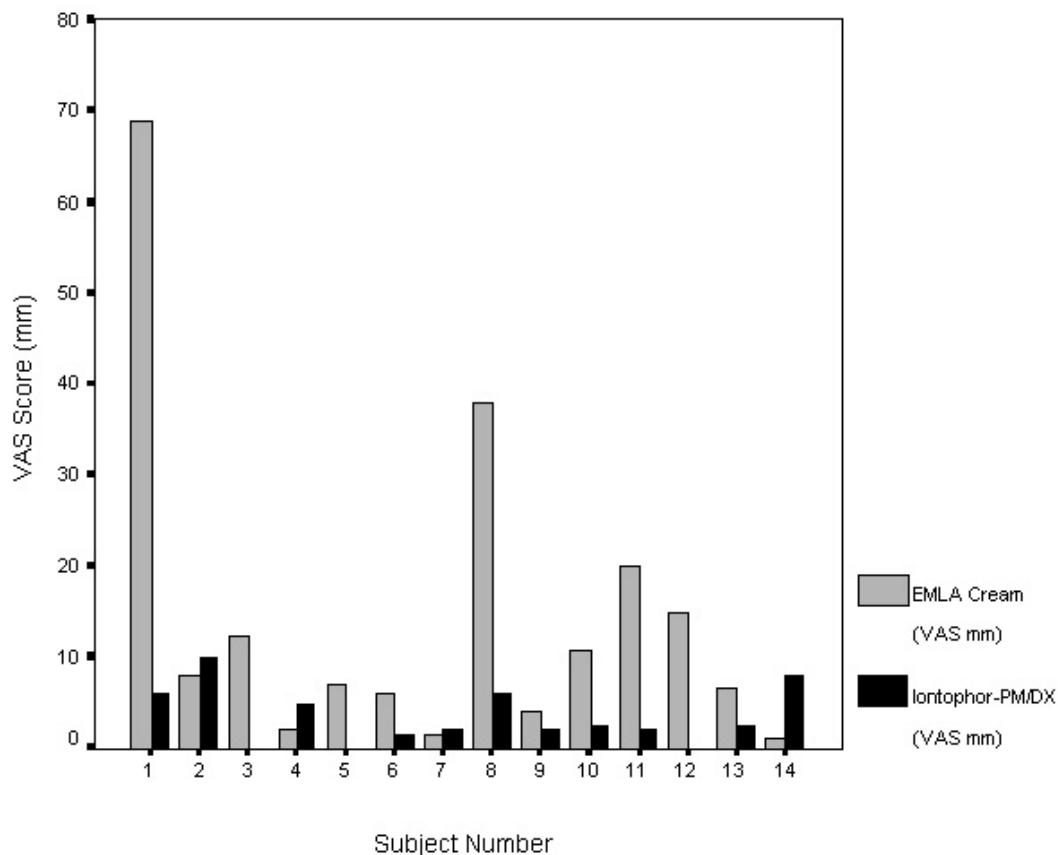
**VAS Scores: Microphor“ Iontophoresis Unit and EMLA Cream Minimum and Maximum (mm)**

	N	Range	Minimum	Maximum	Mean	S.D.
<b>EMLA</b>	15	86	1	87	27	26
<b>Iontophoresis</b>	15	58	10	68	37	19

Near the end of this data collection, it became apparent that the results were not consistent with data reported by previous investigators. The wide ranges of VAS scores for both treatment groups and the large standard deviations were a concern. The batteries in the Iontophoretic unit were replaced and all connections were verified with the manufactures instruction manual. The author questioned whether the MicroPhor™ unit was working properly. Life-Tech, Inc. was contacted. The unit was returned and they verified our concern that the Microphor™ unit was not functioning. They then provided a different unit, the Iontophor™-PM/DX. This unit, although different from the MicroPhor™ unit, was fully programmable and allowed for a more precise delivery of current and dose time to the subject. Because data from the initial sample were not valid, a new data collection process was started utilizing this unit.

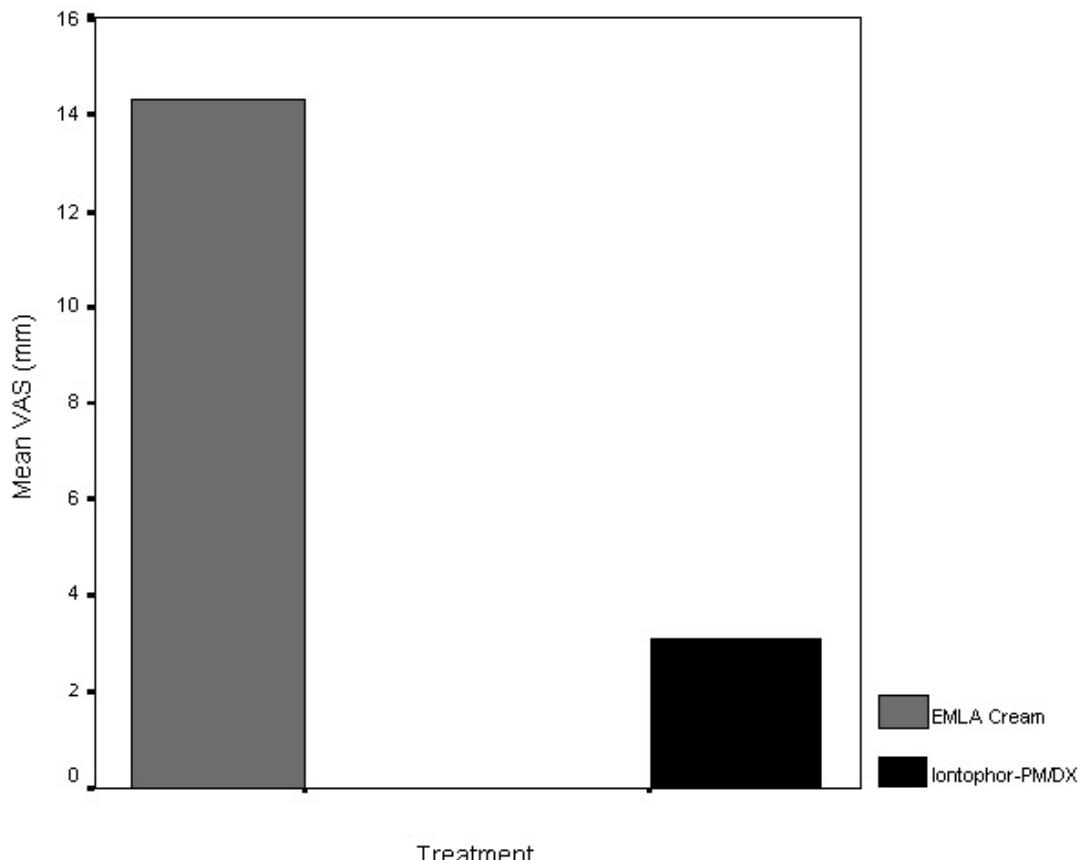
#### Data Analysis: Iontophor™-PM/DX and EMLA Cream

Fourteen different volunteers were enrolled in the study utilizing the Iontophor™-PM/DX unit, eight males and six females. Results of the data collection are presented in Figures 6 and 7.



**Figure 6.**

**VAS Scores for the Iontophor“ -PM/DX and EMLA Cream Group.**



**Figure 7.**

**Mean VAS Scores for the Iontophor-PM/DX Unit and EMLA Cream Group.**

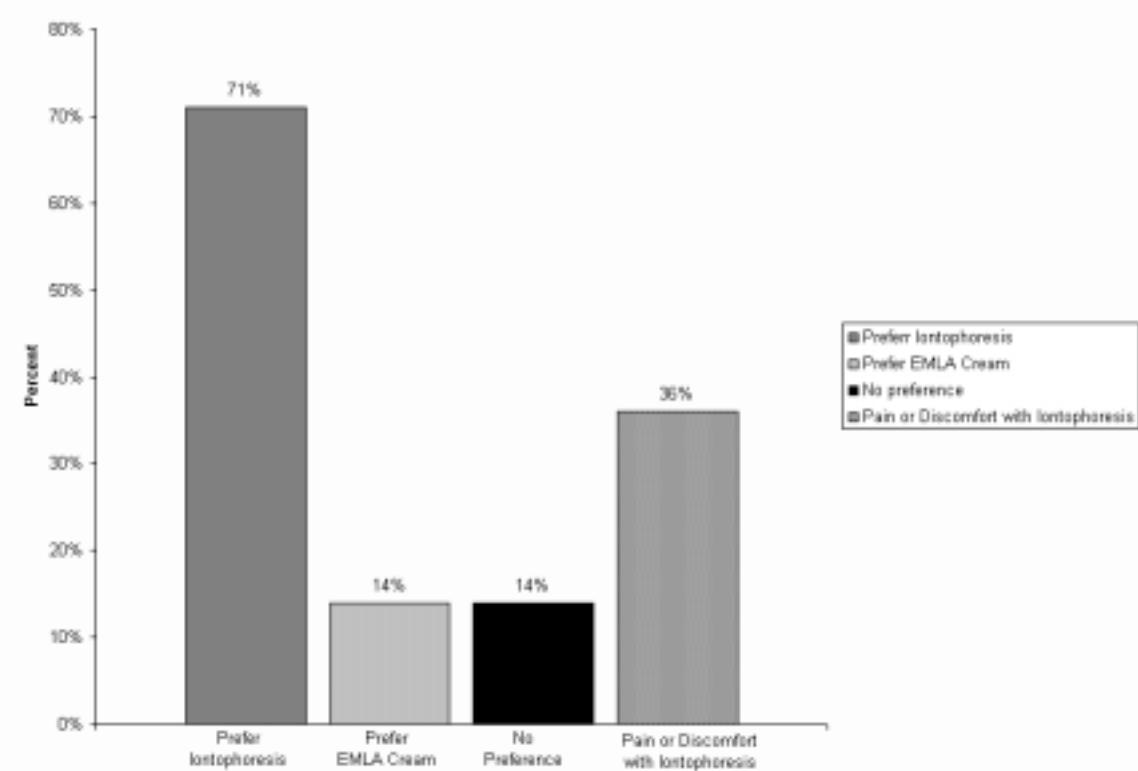
The mean VAS scores for the EMLA group was 14 mm (S.D. 18 mm). The mean VAS score for the Iontophoresis group was 3 mm (S.D. 3 mm). Descriptive statistics are presented in Table 2.

**Table 2:**

**VAS Scores, EMLA Cream and Iontophor“-PM/DX Iontophoresis Unit**

	N	Range	Minimum	Maximum	Mean	Std. Deviation
<b>EMLA</b>	14	68	1	69	14	18
<b>Iontophoresis</b>	14	10	0	10	3	3

To answer the question, Is iontophoresis of 4% lidocaine HCl with Epinephrine 1:50,000 or EMLA cream preferred by adults before intravenous cannulation, subjects were asked to provide comments in writing about the two treatment methods (Appendix D) they received. The qualitative data was analyzed for overall positive, negative or neutral comments, as well as for major themes. There data are presented in Figure 8.



**Figure 8.**

**Frequency Distribution of Written Responses to Treatment Preference.**

The majority of subjects (71%,  $n=10$ ) preferred iontophoresis method to EMLA cream for topical anesthesia prior to IV placement. The remaining four subjects preferred the EMLA (14%,  $n=2$ ) cream or had no preference (14%,  $N=2$ ). One common theme in many of the written responses included pain and or discomfort with the iontophoresis treatment (36%,  $n=5$ ). Three of the ten subjects who preferred the

iontophoresis method also indicated they had pain or discomfort from the iontophoresis treatment. Two subjects who preferred the EMLA cream also indicated they had pain or discomfort with the iontophoresis treatment.

Inferential Statistics:

**Table 3.**

**Statistical Significance of Mean Differences in VAS Scores: EMLA and Iontophoresis**

	Single sample t-test of null hypothesis					
	<b>t</b>	<b>df</b>	<b>Sig. (2-tailed)</b>	<b>Mean Difference</b>	<b>95% Confidence Interval of the Difference</b>	
					<b>Lower</b>	<b>Upper</b>
<b>EMLA</b>	2.904	13	.012	14.321	3.666	24.977
<b>Iontophoresis</b>	4.068	13	.001	3.393	1.591	5.195

Both methods reduced the pain to IV cannulation. However, the iontophoresis method overall reduced the pain to IV cannulation more effectively than the EMLA cream method ( $p=0.001$ ). There was less variability in VAS scores with the iontophoresis treatment than with the EMLA treatment. These results, along with the analysis of the written comments from Figure 8, indicate that the iontophoresis of 4% Lidocaine HCl with Epinephrine 1:50,000 (20 micrograms/millimeter [mcg/ml]) may reduce pain more effectively than EMLA cream to intravenous cannulation in adults. Further, in this study the iontophoresis method of producing topical anesthesia was the preferred method.

### Discussion

Several additional findings were identified during the data collection process. First is the malfunction of the iontophoresis unit may not be readily identified. Any time electrical equipment is used there is always a potential for it to malfunction. This can lead to injury to the patient, inaccurate results, false positives and negatives. As was identified in this research, data collection was almost complete using the MicroPhor™ iontophoresis unit before it became apparent that the data was not consistent with other studies. The mean VAS scores for the EMLA cream groups in both the initial data collection and the final data collection were consistent at 27 mm and 14 mm, respectively. However, there were wide differences in the mean VAS scores between the Microphor™ and Iontophor™-PM/DX units (37 mm and 3 mm, respectively). The author subsequently found that the unit was not functioning properly. This is an important finding as anesthesia providers could be using a piece of equipment and not be aware that is not working properly until clinical signs are noted. An incidental finding from this research was that several subjects reported having pain or discomfort associated with the iontophoresis treatment.

## CHAPTER V: DISCUSSION & RECOMMENDATIONS

### Introduction

The purpose of this study was to compare the iontophoresis of lidocaine with epinephrine to EMLA cream for producing local anesthesia prior to intravenous cannulation. A descriptive pilot study utilizing the experimental method with a cross over design was used. The specific research questions were answered.

### Research Questions

1. Does iontophoresis of 4% Lidocaine HCl with Epinephrine 1:50,000 (20 micrograms/millimeter (mcg/ml) reduce pain more effectively than EMLA cream to intravenous cannulation in adults?
2. Is iontophoresis of 4% lidocaine HCl with Epinephrine 1:50,000 or EMLA cream preferred by adults before intravenous cannulation?

Results were that the iontophoresis of 4% Lidocaine HCl with Epinephrine 1:50,000 (20 mcg/ml) reduced pain associated with intravenous cannulation in adults more effectively than EMLA cream to (14 mm vs. 3 mm for the EMLA cream and Iontophoresis, respectively). The majority of subjects preferred the iontophoresis of 4% lidocaine HCl with Epinephrine 1:50,000 to EMLA cream prior to intravenous cannulation.

### Limitations

Two additional limitations of this study were identified; first was the failure of the Microphor iontophoresis unit. The second was the pain the subjects experienced with the iontophoresis treatment. Because the data were invalid from the Microphor treatment group, new samples of subjects were enrolled. This reduced the sample size of the study,

and delayed completion of the data collection process. The fact that some subjects did experience pain or discomfort with iontophoresis treatment could have influenced their VAS score indirectly.

### Discussion

The incidence of these side effects (pain or discomfort) was similar to what other investigators have noted, tingling, warmth, itching, and erythema beneath the ground electrode, in their research when utilizing iontophoresis, as well as the manufacture (Zempsky, Anand, Sullivan, Fraser, & Cucina, 1998). Superficial burns have even been reported and may be due to the misuse of this technology or poor electrode construction. Although most subjects in our study reported slight or no discomfort, some did experience burning and pain. One subject after receiving iontophoresis with the Iontophor™-PM/DX group did develop a small superficial burn under the ground electrode. Despite the discomfort, the majority of subjects reported a preference for iontophoresis. These results are similar to the results from the study completed by Kim, Kini, Troshynski, and Henner 1999), in which the majority of their subjects also noted a strong preference to use iontophoresis again.

The result of the iontophoresis treatment in this study were consistent with previous published research on lidocaine iontophoresis. Zempsky et al. (1998) noted less pain with intravenous placement in 42 children aged 7-18 years, after 2% lidocaine with epinephrine compared with placebo therapy. Kim et al. (1999) also noted similar results with 2% lidocaine with 1:100,000 epinephrine as compared to placebo therapy, in children undergoing peripheral intravenous catheter insertion in the emergency department. Both of these studies along with results of our study illustrate the efficacy of

lidocaine iontophoresis in producing dermal anesthesia prior to intravenous line insertion.

This study may be the first to compare lidocaine iontophoresis to EMLA cream for intravenous catheter insertion in adults. The fact that the lidocaine iontophoresis reduced the pain to IV catheter insertion more effectively than EMLA cream, in less than 10 minutes, provides anesthesia providers with another method to produce dermal anesthesia. A drawback of this treatment includes the potential for equipment malfunction, and the discomfort with the iontophoresis treatment, both of which occurred in this study. Another factor not addressed in this research is the cost associated with the iontophoresis treatment. This could be a drawback to anesthesia departments adopting this method of dermal anesthesia. The cost of the iontophoresis treatment could be made up by the time saved as compared to EMLA cream.

The conceptual framework for this research study was Imogene King's (as cited in Evans, 1991) Theory of Goal Attainment. The phenomena of concern in this theory was based on processes and outcomes. The process is mutual goal setting between the nurse and the client, and the outcome is the goal to be obtained that can be measured by a change in behavior. In this study, the process was either the iontophoresis of 4% lidocaine HCl with epinephrine or EMLA cream prior to IV cannulation, and the outcome was the reduction of pain to intravenous cannulation. The results of this study indicate that the process, iontophoresis treatment, achieved the goal, reduction of pain prior to IV cannulation.

### Recommendations

A number of recommendations for future studies were identified during this research. First, a randomized double-blind study for IV cannulation, comparing lidocaine

iontophoresis to saline iontophoresis to EMLA cream, to intradermal lidocaine in a clinical setting such as the pre-operative holding area. A study focusing on the cost analysis of these two methods to determine which method is more feasible in a busy anesthesia practice. Finally, future research efforts should determine additional clinical applications, such as arterial or lumbar punctures, of lidocaine iontophoresis, the minimum total dose required to achieve effective dermal anesthesia, and its efficacy in children.

Although far from perfect, dermal anesthesia by lidocaine iontophoresis offers an attractive alternative to EMLA cream for IV insertion. It was concluded that lidocaine iontophoresis is an effective method of producing dermal anesthesia in adults undergoing PIV placement prior to surgery.

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## APPENDICES

APPENDIX A: Life Tech, Inc Needle Buster Setup Chart & Local Anesthesia Protocol Chart.

APPENDIX B: Visual Analog Scale.

APPENDIX C: Comments Form.

APPENDIX D: Informed Consent.

APPENDIX E: Data Collection.

## APPENDIX A

Life Tech, Inc Needle Buster Setup Chart & Local Anesthesia Protocol Chart

## Life-Tech, Inc.

10920 Kinghurst • Houston, TX 77099  
713-495-9411 • Fax: 713-495-7960 • 1-800-231-9841



### NeedleBuster® Setup Chart Meditrode (6570) and Gel-Trode (6585)

Age	0-2 Yrs.	2-6 Yrs.	6+ Yrs. / Patient Comfort Level	
Current	.5 - 1.5	1.5 - 3	3 - 4	
Time (minutes)	20 - 60		10 - 15	
Meditrode Fluid Capacity	Bandaid 6570S 1.5 CC	Small Square 6570M 2 CC	Round 6570R 6CC	Large 6570S 7CC

#### Skin Preparation

1. Inspect site for skin imperfections.

**Caution:** Do not place electrode over skin imperfections such as moles, scars, warts, or damaged skin. If can not be avoided, insulate damaged area by applying Vaseline with a Q-tip over imperfection only. Clip excessive hair if necessary. Do not shave treatment area within 24 hours before treatment.

2. Wipe with alcohol swab and let dry

**Caution:** Do not abrade



6570(x)

6585(xx)

#### Meditrode Application

1. Remove backing from 6570(x)Meditrode®
2. Apply to clean & dry treatment area, slightly stretching while applying to remove all wrinkles
3. Connect the red NeedleBuster lead wire to the active drug delivery Meditrode® (6570 series)
4. Remove backing from the 6585(xx) self adhering dispersive Gel-Trode
5. Apply to clean & dry treatment area starting from the center and pressing towards the end to smooth all wrinkles
6. Connect the black NeedleBuster® lead wire to the self adhering dispersive Gel-Trode
7. Saturate the 6570(x)active drug delivery Meditrode with drug solution by placing the syringe tip into the fill ports and injecting fluid until electrode saturation is achieved.

Meditrode	Bandaid	Small Square	Round	Large Square
Fluid Capacity	6570S 1.5 CC	6570M 2 CC	6570R 6CC	6570L 7CC

#### NeedleBuster® Connection

1. Connect leads to NeedleBuster® by connecting the red lead to the red connector labeled "Drug (+)" and the black lead to the black connector labeled "RTRN (-)"
2. Turn on NeedleBuster® by pressing the key pad labeled "On/Off" and observing that the "PWR" light is on and the "OPN" light is off. If "OPN" occurs, consult NeedleBuster operating manual.
3. Set Current as shown above by rotating Current knob clockwise to increase delivery time and counter clockwise to decrease delivery time
4. Set Time as shown above by rotating Time knob clockwise to increase delivery time and counter clockwise to decrease delivery time.

### Local Anesthesia Suggested Protocol Chart (Dr. James Hamilton)

#### Meditrode Set Up:

##### Meditrode Size and Capacity\*

Local Anesthetic 2.4%**	Bandaid	1.5 cc	Small Square 2.0 cc	Round 6 cc	Large Square 7 cc	* Saturate until weeping from fill port is observed.
		1.25 cc	1.75 cc	3 cc	3 cc	** If vasoconstrictor is omitted, increase local anesthetic for maximum saturation.
Vasoconstrictor 1:10,000- 1:200,000		0.25	25 cc	1 cc	1 cc	

#### Unit Set Up:

##### Age Group

##### 2-6 Years

##### 6 + Years

##### After adding medication, add de-ionized or sterile water to saturate Round

##### or Large Square. If child is 2-6 years, follow time & current for Small Square.

##### (patient comfort level)

##### Current

##### 0.5-1 mA

##### 2 mA

##### 2-4 mA

##### Time (min)

##### 20-15 min

##### 10 min

##### 10, 7.5, 5 min

Important: Life-Tech, Inc., does NOT endorse or recommend the use of the Tontophor system with any medications, chemicals or substances. The Protocols are recommendations or experts in the field, supplied at your request. Life-Tech does NOT endorse or recommend modification or use of the NeedleBlaster system in a manner other than specifically shown in the operating manual.

APPENDIX B  
Visual Analog Scale

### Visual Analogue Scale

This is a scale representing your pain. The left end represents no pain at all, and the right end represents pain as bad as it could possibly be. Mark a point somewhere on this scale that represents where your pain level is at this moment.



Date: \_\_\_\_\_

Time: \_\_\_\_\_

Subject Number: \_\_\_\_\_

Degree of difficulty with venipuncture:

1=easy      2=moderately easy      3= difficult      4= very difficult

## APPENDIX C

### Comments Form

Please use this form to write down any comments that you can provide us about the two treatment measures you just received. Specifically comment on which method of producing local anesthesia you preferred, and why. Also, comment on whether you would use Iontophoresis or EMLA cream again.

Date: \_\_\_\_\_

Time: \_\_\_\_\_

Subject Number: \_\_\_\_\_

## APPENDIX D

### Informed Consent

## Informed Consent Form

### Research Study

#### A COMPARISON OF THE IONTOPHORESIS OF LIDOCAINE WITH EPINEPHRINE TO EMLA CREAM FOR REDUCTION OF PAIN TO INTRAVENOUS CANNULATION IN ADULTS

My name is LTJG Kenneth L. Spence. I am a Nurse Anesthesia graduate student conducting research for my master's thesis. You are being asked to take part in a research study. Before you decide to be a part of this research study, you need to understand the risks and benefits so that you can make an informed decision. This is known as informed consent. This consent form provides information about the research study, which has been explained to you. Once you understand the study and the tests it requires, you will be asked to sign this form if you desire to participate in the study. Your decision to participate is voluntary. This means that you are free to choose if you will take part in the study.

#### Purpose and Procedures

The Department of Nursing Anesthesia of the Uniformed Services University of the Health Sciences is carrying out this research study to find out whether the use of a small electric current to deliver a local anesthetic across the skin is more or less effective than a topically applied local anesthetic to reduce the pain of intravenous cannulation in adults. Twenty volunteers will be asked to participate in this research study. Iontophoresis is the process of delivering a medication across the skin using an electric current. EMLA cream is a topical numbing medication used prior to placing an intravenous catheter.

The procedure for this study includes the application of the EMLA cream to the top of a randomly selected hand with a clear tegaderm cover placed over the medication. This will be left in place for 60 minutes. After that time the cream will be wiped off your skin and an intravenous catheter will be inserted into a suitable vein under the treatment area. After a flash back of blood is noted in the needle hub, you will be asked to rate your pain on a Visual Analog Scale.

The iontophoresis procedure will consist of the application of an electrode to the top surface of your contralateral hand and then the electrode will be saturated with a solution of lidocaine and epinephrine. Another electrode will be placed further down your arm, and then two electrical wires will be attached to the electrodes. An electric current will be used to deliver the medication across your skin. You may feel a slight tingle as the current is being delivered. This procedure should take no more than 15 minutes. After this procedure is completed an intravenous catheter will be inserted into a suitable vein and then you will be asked to rate your pain on a Visual Analog Scale.

In addition you will be asked the following question: Please use this form to write down any comments that you can provide us about the two treatment measures you just

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**JUNE 29, 1998;**

**IRB. PROTOCOL NUMBER: T06158-01**

**SUBJECT INITIALS \_\_\_\_\_**

**WITNESS INITIALS \_\_\_\_\_**

received. Specifically comment on which method of producing local anesthesia you preferred, and why. Also, comment on whether you would use Iontophoresis or EMLA cream again.

### **Benefits**

There is no direct benefits to participating in this study.

### **Time Commitment**

The time commitment for this study will consist of one 60-90 minute session during which both procedures will be accomplished.

### **Risks, Inconveniences, Discomforts**

The potential risks of this study may include: temporary redness of the iontophoretically treated site, minor stinging or burning sensations. Other potential risks include, bruising at the intravenous site, failure to produce adequate pain relief, and potential allergic reaction to the local anesthetics used. You may experience some anxiety with the venipuncture.

### **Cost of Participation**

None to you.

### **Alternatives**

The alternative is to not participate in this research study.

### **Voluntariness**

Participation is voluntary, refusal to participate will involve no penalty or loss of benefits, and you may discontinue participation at any time without penalty or loss of benefits. Inclusionary criteria: Twenty Nurse Anesthetist Student volunteers will be recruited to participate in this study. Exclusionary criteria: No subject who has allergies to any of the medications being utilized in this study will be asked to participate.

### **Research Related Injury**

This study should not entail any physical or mental risk beyond those described above. We do not expect complications to occur, but if, for any reason, you feel that continuing this study would constitute a hardship for you, we will end your participation in the study.

DoD will provide medical care at government facilities for any DoD eligible for injury or illness resulting from participation in this research. Such care may not be available to other research participants. Compensation may be available through judicial avenues to non-active duty research participants if they are injured through the negligence (fault) of the Government.

If at any time you believe you have suffered an injury or illness as a result of participating in this research project you should contact the Office of Research Administration at the Uniformed Services University of the Health Sciences, Bethesda, MD 20814 at (301) 295-3303. This office can review the matter with you, can provide you information about your rights as a subject, and may be able to identify resources available to you. Information about judicial avenues of compensation is available from the University's General Counsel (301) 295-3028.

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**JUNE 29, 1998**

**IRB. PROTOCOL NUMBER: T06158-01**

**SUBJECT INITIALS \_\_\_\_\_**

**WITNESS INITIALS \_\_\_\_\_**

### **Confidentiality of Records**

All information that you provide as a part of this study will be confidential and will be protected to the fullest extent of the law. Information that you provide and other records related to this study will be kept private, accessible only to those persons directly involved in conducting this study and members of the Uniformed Services University of the Health Sciences Institutional Review Board, who provide oversight for human use protection. All questionnaires and forms will be kept in a restricted access, locked cabinet while not in use. However, please be advised that under UCMJ, a military member's confidentiality cannot be strictly guaranteed. To enhance the privacy of your responses you will not be identified on any of the data collection tools utilized. Any reports generated from this study will not divulge your name or identity.

### **Withdrawal**

I understand that I may at any time during the course of this research study revoke my consent, and withdraw from the study without prejudice. I have been given an opportunity to ask questions concerning this research study, and any such questions have been answered to my complete satisfaction. Call LTJG Kenneth L. Spence at 301-540-3721, if you have any concerns, questions, or Maura S. McAuliffe Ph.D., CRNA at 301-295-6565, chair of my thesis committee. If you have any questions about your rights as a research subject, you should call the Director of Research Programs in the Office of Research at the Uniformed Services University of the Health Sciences at (301) 295-3303. This person is your representative and has no connection to the researchers conducting this study.

I do hereby volunteer to participate in a research study entitled: A COMPARISON OF THE IONTOPHORESIS OF LIDOCAINE WITH EPINEPHRINE TO EMLA CREAM FOR REDUCTION OF PAIN TO INTRAVENOUS CANNULATION. The implications of my voluntary participation: the nature, duration and purpose; the methods and means by which it is to be conducted; and the inconveniences and hazards to be expected have been thoroughly explained to me by

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By signing this consent form you are agreeing that the study has been explained to you and that you understand this study. You are signing that you agree to take part in this study. You will be given a copy of this consent form.

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**JUNE 29, 1998**

**IRB. PROTOCOL NUMBER: T06158-01**

**SUBJECT INITIALS \_\_\_\_\_**

**WITNESS INITIALS \_\_\_\_\_**

I have been given the opportunity to ask questions concerning this study, and any such questions have been answered to my full and complete satisfaction.

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Name (print)

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Date

---

Signature

---

Date

---

Signature (witness)

---

Date

I Certify that the research study has been explained to the above individual, by me, and that the individual understands the nature and purpose, the possible risks and benefits associated with taking part in this research study. Any questions that have been raised have been answered.

---

Investigator

---

Date

---

**JUNE 25, 1998**

**IRB. PROTOCOL NUMBER: T06158-01**

**SUBJECT INITIALS\_\_\_\_\_**

**WITNESS INITIALS\_\_\_\_\_**

## APPENDIX E

### Data Collection

### EMLA Cream and Microphor Data

Subject #	EMLA (VAS mm)	Iontophoresis (VAS mm)	Gender
1	83.0	35.0	Male
2	15.0	47.0	Male
3	17.0	35.0	Male
4	34.0	15.0	Male
5	87.0	65.0	Female
6	15.0	28.0	Male
7	31.0	47.0	Female
8	13.0	68.0	Male
9	20.0	23.0	Female
10	42.0	36.0	Female
11	2.0	10.0	Male
12	11.0	66.0	Female
13	40.0	14.0	Female
14	5.0	22.0	Female
14	1.0	45.0	Female

### EMLA Cream and Iontophor-PM/DX Data

Subject #	EMLA (VAS mm)	Iontophoresis (VAS mm)	Gender
1	69	6	Male
2	8	10	Male
3	12	0	Male
4	2	5	Male
5	7	0	Female
6	6	1.5	Male
7	1.5	2	Female
8	38	6	Male
9	4	2	Female
10	10.5	2.5	Female
11	20	2	Male
12	15	0	Female
13	6.5	2.5	Female
14	1	8	Female

## Thesis Comments

Subject # 1: With iontophoresis the initial current felt like a burn as it approached 4mA. After awhile I could tell a current was still there but it was not as uncomfortable as in the beginning. I felt the sensation get worse as the current was turned down at the end of the study. I would prefer the iontophoresis to EMLA cream just because at venipuncture I felt very little with the iontophoresis.

Subject # 2: EMLA/ Iontophoresis works equally

Subject # 3: I preferred iontophoresis because I didn't feel anything when the needle was inserted. I was pleasantly surprised at the results since I've always been an EMLA cream advocate; especially with pediatric cases. I think iontophoresis is time effective as well which is a big plus in the present days when everyone wants the patient ready to go to the OR NOW!

Subject # 4: My preference is the EMLA cream. There are several reasons for this preference. Neither procedure is effective for emergency procedures. The iontophoresis method is an interesting concept, but appears bulky, time consuming on the part of the practitioner, and less effective for pain control. I received a constant sting at both the positive and negative ground sites. The ground pad left a tender to touch irritation (electrical burn) that was still nonetheless uncomfortable. I don't think its efficacy with children is valid secondary to the wires and need for an external mechanical device.

The EMLA cream provided better pain control upon catheter insertion. It would appear that a pediatric patient would tolerate this method secondary to the increased freedom prior to ht catheter insertion, and increased efficacy.

Subject # 5: There wasn't a-lot of discomfort with either stick. The electrical treatment though was pain free, completely needless doesn't bother me and I think I have a good pain threshold, but I would recommend a pain free method for someone that is really nervous about getting stuck. I was on an IV team and when people are nervous, their veins disappear. Between the two methods used, today the iontophoresis method was quicker and less messy.

Subject # 6: Iontophoresis is more convenient due to rapid administration of anesthetic. However, I felt a slight amount of discomfort when the charge was applied. The iontophoresis provided better anesthesia, therefore, it would be my choice.

Subject # 7: Both methods reduced discomfort. The EMLA cream takes longer to work- often the luxury of time is not available. The iontophoresis was faster and worked almost as well. It would work well with kids-no needles and not much more time needed than with injection of lidocaine. The iontophoresis gave an interesting sensation-like touching an electric fence with a long piece of grass-a buzz, but no pain.

Subject # 8: Iontophoresis was uncomfortable at first but much more effective with decreasing pain at puncture. EMLA cream was very unsuccessful at preventing pain relief. Iontophoresis would be an option for painful type punctures.

Subject # 9: I thought the iontophoresis was the better method of the two. It didn't take as long to set up and actually I felt less pain on IV insertion with this method. The EMLA cream was sufficient for pain control but it was messy and took 45" to work. I did feel more of a "stick" when the IV was started. I would definitely use the iontophoresis and probably the EMLA too, depending on the situation.

Subject # 10: The electrode treatment did not hurt at all. The EMLA cream site did not hurt as much as electrode treatment. Overall, both sides did not hurt much; Unlike IV starts with out any thing or with a poke of lidocaine first.

Subject # 11: Definitely more analgesia with iontophoresis. Even though it was more burdensome to set up, I would consider using it.

Subject # 12 The iontophoresis was preferred. There was no sensation of pain or pressure, though some "tingling" sensation during the iontophoresis preparation. The EMLA cream IV start felt the same as if no local anesthesia was used.

Subject # 13: Iontophoresis less painful, EMLA cream took longer. Would use iontophoresis again.

Subject # 14: I prefer EMLA cream because I felt nothing and the iontophoresis was extremely uncomfortable (burning and stinging) along with a small burn from that. I would have rather felt a stick.